

AMENDMENTS TO THE CLAIMS

1. (withdrawn) A method of diagnosing or prognosticating a neurodegenerative disease in a subject, or determining whether a subject is at increased risk of developing said disease, comprising:

determining a level and/or an activity of

(i) a transcription product of the TB2 gene, and/or

(ii) a translation product of the TB2 gene, and/or

(iii) a fragment, or derivative, or variant of said transcription or translation product in a sample from said subject and comparing said level and/or said activity to a reference value representing a known disease or health status, thereby diagnosing or prognosticating said neurodegenerative disease in said subject, or determining whether said subject is at increased risk of developing said neurodegenerative disease.

2. (withdrawn) The method according to claim 1 wherein said neurodegenerative disease is Alzheimer's disease.

3. (withdrawn) A kit for diagnosing or prognosticating a neurodegenerative disease in a subject, or determining the propensity or predisposition of a subject to develop such a disease, said kit comprising:

(a) at least one reagent which is selected from the group consisting of (i) reagents that selectively detect a transcription product of the TB2 gene and (ii) reagents that selectively detect a translation product of the TB2 gene; and

(b) an instruction for diagnosing or prognosticating a neurodegenerative disease, or determining the propensity or predisposition of subject to develop such a disease by (i) detecting a

level, or an activity, or both said level and said activity, of said transcription product and/or said translation product of the TB2 gene, in a sample from said subject; and (ii) diagnosing or prognosticating a neurodegenerative disease, or determining the propensity or predisposition of said subject to develop such a disease, wherein a varied level, or activity, or both said level and said activity, of said transcription product and/or said translation product compared to a reference value representing a known health status; or a level, or activity, or both said level and said activity, of said transcription product and/or said translation product similar or equal to a reference value representing a known disease status indicates a diagnosis or prognosis of a neurodegenerative disease, or an increased propensity or predisposition of developing such a disease.

4. (withdrawn) A modulator of an activity and/or of a level of at least one substance which is selected from the group consisting of:

- (i) the TB2 gene,
- (ii) a transcription product of the TB2 gene, and
- (iii) a translation product of the TB2 gene, and
- (iv) a fragment, or derivative, or variant of (i) to (iii).

5. (withdrawn) A recombinant, non-human animal comprising a non-native gene sequence coding for TB2 or a fragment, or a derivative, or a variant thereof, said animal being obtainable by:

- (i) providing a gene targeting construct comprising said gene sequence and a selectable marker sequence, and
- (ii) introducing said targeting construct into a stem cell of a non-human animal, and
- (iii) introducing said non-human animal stem cell into a non-human embryo, and

- (iv) transplanting said embryo into a pseudopregnant non-human animal, and
- (v) allowing said embryo to develop to term, and
- (vi) identifying a genetically altered non-human animal whose genome comprises a modification of said gene sequence in both alleles, and
- (vii) breeding the genetically altered non-human animal of step (vi) to obtain a genetically altered non-human animal whose genome comprises a modification of said endogenous gene, wherein said disruption results in said non-human animal exhibiting a predisposition to developing symptoms of a neurodegenerative disease or related diseases or disorders.

6. (withdrawn) A method for screening for a modulator of neurodegenerative diseases, or related diseases or disorders of one or more substances selected from the group consisting of:

- (i) the TB2 gene,
- (ii) a transcription product of the TB2 gene,
- (iii) a translation product of the TB2 gene, and
- (iv) a fragment, or derivative, or variant of (i) to (iii),

said method comprising:

- (a) contacting a cell with a test compound;
- (b) measuring the activity and/or level of one or more substances recited in (i) to (iv);
- (c) measuring the activity and/or level of one or more substances recited in (i) to (iv) in a control cell not contacted with said test compound; and

- (d) comparing the levels and/or activities of the substance in the cells of step (b) and (c), wherein an alteration in the activity and/or level of substances in the contacted cells indicates that the test compound is a modulator of said diseases or disorders.

7. (withdrawn) A method of screening for a modulator of neurodegenerative diseases, or related diseases or disorders of one or more substances selected from the group consisting of

- (i) the TB2 gene,
- (ii) a transcription product of the TB2 gene,
- (iii) a translation product of the TB2 gene, and
- (v) a fragment, or derivative, or variant of (i) to (iii),

said method comprising:

- (a) administering a test compound to a test animal which is predisposed to developing or has already developed symptoms of a neurodegenerative disease or related diseases or disorders in respect of the substances recited in (i) to (iv);

- (b) measuring the activity and/or level of one or more substances recited in (i) to (iv);

- (c) measuring the activity and/or level of one or more substances recited in (i) to (iv) in a matched control animal which is predisposed to developing or has already developed symptoms of a neurodegenerative disease or related diseases or disorders in respect to the substances recited in (i) to (iv) and to which animal no such test compound has been administered;

- (d) comparing the activity and/or level of the substance in the animals of step (b) and (c), wherein an alteration in the activity and/or level of substances in the test animal indicates that the test compound is a modulator of said diseases or disorders.

8. (withdrawn) The method according to claim 7 wherein said test animal and/or said control animal is a recombinant animal which expresses a gene coding for TB2, or a fragment, or a derivative, or a variant thereof, under the control of a transcriptional control element which is not the native TB2 gene transcriptional control element.

9. (previously presented) An assay for testing a compound for inhibition of binding between a ligand and a translation product of the gene coding for ~~TB2~~ the amino acid sequence of SEQ ID No. 1, or a fragment, or derivative, or variant thereof, said assay comprising the steps of:

(i) adding a liquid suspension of said ~~TB2~~-translation product of the gene coding for the amino acid sequence of SEQ ID No. 1 to a plurality of containers;

(ii) adding a compound or a plurality of compounds to be screened for said inhibition to said plurality of containers;

(iii) adding a detectable, labeled ligand to said containers;

(iv) incubating said ~~TB2~~ translation product of the gene coding for the amino acid sequence of SEQ ID No. 1, or said fragment, or derivative, or variant thereof, and said compound or compounds, and said labeled ligand;

(v) measuring amounts of detectable label associated with said ~~TB2~~ translation product of the gene coding for the amino acid sequence of SEQ ID No. 1, or with said fragment, or derivative, or variant thereof; and

(vi) using the measured amounts of detectable label to determine ~~determining~~ the degree of inhibition by one or more of said compounds of binding of said ligand to said ~~TB2~~ translation

product of the gene coding for the amino acid sequence of SEQ ID No. 1, or said fragment, or derivative, or variant thereof.

10. (withdrawn) The method of claim 1, comprising determining a level and/or an activity of a protein molecule shown in SEQ ID NO. 1, said protein molecule being a translation product of the gene coding for TB2, or a fragment, or derivative, or variant thereof.

11. (withdrawn) The method of claim 6, wherein said screening is for a modulator of a protein molecule shown in SEQ ID NO. 1, said protein molecule being a translation product of the gene coding for TB2, or a fragment, or derivative, or variant thereof, wherein said modulator is a reagent or compound for preventing, or treating, or ameliorating a neurodegenerative disease.

12. (withdrawn) A method of detecting a pathological state of a cell in a sample from a subject, said method comprising staining said cell by immunocytochemical staining with an antibody specifically immunoreactive with an immunogen, wherein said immunogen is a translation product of the gene coding for TB2, SEQ ID NO. 1, or a fragment, or derivative, or variant thereof, wherein an altered degree of staining, or an altered staining pattern in said cell compared to a cell representing a known health status indicates a pathological state of said cell.

13. (withdrawn) The kit of claim 3, wherein said neurodegenerative disease is Alzheimer's disease.

14. (withdrawn) A pharmaceutical composition comprising the modulator of claim 4.

15. (withdrawn) The method of claim 6, wherein said neurodegenerative disease is Alzheimer's disease.

16. (withdrawn) The method of claim 7, wherein said neurodegenerative disease is Alzheimer's disease.

17. (previously presented) The assay of claim 9, wherein said assay is for screening a plurality of compounds for inhibition of binding between a ligand and a translation product of the gene coding for ~~TB2~~ the amino acid sequence of SEQ ID No. 1, or a fragment, or a derivative, or a variant thereof.

18. (previously presented) The assay of claim 9, wherein the detectable, labeled ligand is a fluorescently labeled ligand.

19. (previously presented) The assay of claim 9, wherein the detectable label is ~~fluorescence~~ fluorescent.

20. (withdrawn) The method of claim 10, wherein the neurodegenerative disease is Alzheimer's disease.

21. (withdrawn) The method of claim 11, wherein the neurodegenerative disease is Alzheimer's disease.

22. (withdrawn) The method of claim 7, wherein said screening is for a modulator of a protein molecule shown in SEQ ID NO. 1, said protein molecule being a translation product of the gene coding for TB2, or a fragment, or derivative, or variant thereof, wherein said modulator is a reagent or compound for preventing, or treating, or ameliorating a neurodegenerative disease.

23. (withdrawn) The method of claim 22, wherein the neurodegenerative disease is Alzheimer's disease.

24. (previously presented) The ~~method~~ assay of claim 9, wherein said assay is for testing a compound for inhibition of binding between a ligand and a protein molecule shown in SEQ ID NO. 1, said protein molecule being a translation product of the gene coding for TB2, or a fragment, or derivative, or variant thereof, wherein said compound is for preventing, or treating, or ameliorating a neurodegenerative disease.

25. (previously presented) The ~~method~~ assay of claim 24, wherein the neurodegenerative disease is Alzheimer's disease.